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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/522,911 | 07/07/2005 | Peter D Senter | SGEN-0051/1000-00212US | 7034 |

23377 7590 04/29/2008

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| EXAMINER | |
|---|---|
| BRADLEY, CHRISTINA | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1654 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 04/29/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/522,911 | SENTER ET AL. | |
| | Examiner | Art Unit | |
| | Christina Marchetti Bradley | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7,9,17-21,27,54,63,66,79,111-121 and 123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/7/05,12/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,7,9,17-30,44-46,48,49,52,54,56,59,63,66,77,79,100,104 and 111-123.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 22-26,28-30,44-46,48,49,52,56,59,77,100,104 and 122.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of the species depicted in claim 79 wherein L is an anti-CD30 antibody and p is 4 in the reply filed on 12/19/2007 is acknowledged. Claims 1, 2, 7, 9, 17-30, 44-46, 48, 49, 52, 54, 56, 59, 63, 66, 77, 79, 100, 104 and 111-123 are pending; claims 22-26, 28-30, 44-46, 48, 49, 52, 56, 59, 77, 100, 104 and 122 are withdrawn for pertaining to a non-elected species. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-121 and 123 are examined on the merits.

### *Specification*

2. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Complete revision of the content of the abstract is required on a separate sheet. The revision should include a recitation of the general nature of the claimed drugs.

3. The use of the trademark Chromatotron has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-121 and 123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to compounds of Formula 1a and solvates thereof. In paragraph 0383 of the specification, solvates are defined as "an association of one or more solvent molecules and a Compound of the Invention." According to the specification, examples "of solvents that form pharmaceutically acceptable solvates include, but are not limited to, water, isopropanol, ethanol, methanol, DMSO, ethyl acetate, acetic acid, and ethanolamine." Beyond this generic description of solvates, the specification fails to describe the structural, physical and functional properties of a single specific solvate of a compound of Formula 1a. The specification further fails to provide guidance on how to obtain specific solvates with the disclosed functional properties of compounds of Formula 1a. A description of these properties is essential to demonstrate possession of the genus of solvates given the state of the art at the time of filing. The prior art suggests that solvates can have unique properties that differ significantly from the

compounds. For example, Vippagunta *et al. Adv. Drug Delivery Rev.*, **2001**, *48*, 3-26) teach that, "Because different crystalline polymorphs and solvates differ in crystal packing, and/or molecular conformation as well as in lattice energy and entropy, there are usually significant differences in their physical properties, such as density, hardness, stability, refractive index, melting point, enthalpy of fusion, vapor pressure, solubility, dissolution rate, other thermodynamic and kinetic properties and even color. Differences in physical properties of various solid forms have an important effect on the processing of drug substances into drug products, while differences in solubility may have implications on the absorption of the active drug from its dosage form, by affecting the dissolution rate and possibly the mass transport of the molecules." (page 4). Given that solvates can have unique physical and functional properties, Applicant must outline these properties in order to demonstrate full possession of the genus. In the instant case, only a generic definition of pharmaceutically acceptable solvates is provided. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

6. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-121 and 123 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and are as follows:

*The Nature of the Invention*

The claims are drawn to compounds of Formula 1a and solvates thereof.

*The State of the Prior Art and its Predictability or Unpredictability*

The prior art establishes that the formulation of pharmaceutical compounds as solvates is highly unpredictable. Vippagunta *et al.* (*Adv. Drug Delivery Rev.*, **2001**, *48*, 3-26) teach that, "The common crystalline forms found for a given drug substance are polymorphs and solvates." (page 4). "Solvates, also known as pseudopolymorphs, are crystalline solid adducts containing solvent molecules within the crystal structure, ... giving rise to unique differences in the physical and pharmaceutical properties of the drug. If the incorporated solvate is water, a solvate is termed a hydrate." (page 4).

Vippagunta *et al.* teach that, "Because different crystalline polymorphs and solvates differ in crystal packing, and/or molecular conformation as well as in lattice energy and entropy, there are usually significant differences in their physical properties, such as density, hardness, tabletability, refractive index, melting point, enthalpy of fusion, vapor pressure, solubility, dissolution rate, other thermodynamic and kinetic properties and even color. Differences in physical properties of various solid forms have an important effect on the processing of drug substances into drug products, while differences in solubility may have implications on the absorption of the active drug from its dosage form, by affecting the dissolution rate and possibly the mass transport of the molecules." (page 4).

Vippagunta *et al.* teach that, "It is very important to control the crystal form of the drug during the various drug development, because any phase change due to polymorph interconversions, desolvation of solvates, formation of hydrates and change in the degree of crystallinity can alter the bioavailability of the drug. When going through a phase transition, a

solid drug may undergo a change in its thermodynamic properties, with consequent changes in its dissolution and transport characteristics." (page 5).

Vippagunta *et al.* teach that "Phase changes due to hydration/dehydration and solvation/desolvation of pharmaceutical compounds during processing or in the final product may result in an unstable system that would effect the bioavailability of drug from solid dosage forms. Various types of phase changes are possible in solid-state hydrated or solvated systems in response to changes in environmental conditions… For example, some hydrated compounds may convert to an amorphous phase upon dehydration and some may convert from a lower to a higher state of hydration yielding forms with lower solubility. Alternatively, a kinetically favored but thermodynamically unstable form may be converted during pharmaceutical processing to a more stable and less soluble form." (page 17).

Vippagunta *et al.* that, "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds… There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates." (page 18).

*The Relative Skill of Those in the Art*

The relative skill of those in the art is high.

*The breadth of the claims*

In paragraph 0383 of the specification, solvates are defined as "an association of one or more solvent molecules and a Compound of the Invention." According to the specification,

examples "of solvents that form pharmaceutically acceptable solvates include, but are not limited to, water, isopropanol, ethanol, methanol, DMSO, ethyl acetate, acetic acid, and ethanolamine."

*The Amount of Direction or Guidance Presented and the Presence of Working Examples*

The specification fails to provide a single working example demonstrating that the claimed compounds can be formulated as solvates. The specification further fails to provide guidance on how to produce solvates of formula 1a that maintain the disclosed functional properties of the compounds.

*The Quantity of Experimentation Necessary*

Considering the factors above, the skilled artisan would be burdened with undue experimentation in determining if one of the claimed compounds could be formulated as a solvate. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

7. Claims 111-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and are as follows:

*The nature of the invention*

The invention is in the field of pharmaceuticals, and provides drug conjugates as prodrugs for the delivery of drugs to cell populations, where the prodrugs are metabolized and

activated by endogenous enzymes to provide active drugs. Claims 111-119 are drawn to pharmaceutical compositions for and methods of treating tumors, cancer, autoimmune disorders and infectious diseases.

*The State of the Prior Art and its Predictability or Unpredictability*

It is well known in the art that for cancer therapy, while drugs may be effective *in vitro* and in mice, they are not necessarily effective in humans. For example, Dermer (*Bio/Technology*, **1994**, *12*, 320) states that "immunotherapy's killing power of the transformation of 3T3 cells by a mutated protooncogene, simply does not have the same significance for cells *in vivo*.' (See page 320). Further, "[t]he facts indicate, however, that petri dish cancer is really poor representation of malignancy, with characteristics profoundly different from human disease." (See page 320). Similar sentiments are echoed in a Science article by Trisha Gura (*Science*, **1997**, *278*, 1041-2). The article indicates that the fundamental problem in cancer research is that model systems are not predictive of *in vivo* activity (see page 1041). The article goes on to state that xenograft models in mice "don't behave like naturally occurring tumors in humans--they don't spread to other tissues." (See page 1041). Further, other systems such as clonogenic assays are not always helpful since they "can't always predict how a tumor will respond to a drug in an animal" and "[s]omedmes they don't work because the cells simply fail to divide n culture." (See page 1042). In essence, the art indicates that "rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer or diseases of the central nervous system." (See page 44 of Golden, *Time*, **1998**, *May 18*).

*The relative skill of those in the art*

The relative skill of the those in the art is high.

*The breadth of the claims*

The method claims are drawn a method of treating cancer and a method for killing or inhibiting the multiplication of tumor or cancer cells by the administration a compound of claim 1. The method claims are additionally drawn to methods of treating an autoimmune disease and an infectious disease.

*The amount of direction or guidance presented and the presence or absence of working examples*

The specification sets forth a general disclosure of disease and cancers that can be treated using the compounds of the claimed invention. The specification recites agents that are known to be useful in the treatment of certain cancer. The specification also presents data on drugs conjugated to two specific monoclonal antibodies, cBR$^{96}$ and cAC10, and their effect on *in vivo* human lung adenocarcinoma, Karpas human anaplastic cell lymphoma and Hodgkin's Disease xenograft models. However the claims are not limited to those monoclonal antibodies or cancers. Rather the claims are open to any ligand and the treatment of any disease or cancer. While the specification list numerous ligands, the specification does not provide guidance whether such ligand can be used to treat the innumerable number of cancers encompassed by the claims. The specification lists *in vitro* cytotoxic assay methods. However, the specification fails to provide any data obtained using the compounds of the claimed invention. Note that one cannot readily conclude whether the claimed compounds will behave the same as the native biologically active compound. The claimed molecules contain large moieties that can effect biological activities. It is well known in the art that small changes in the chemical composition of a biological agent can have adverse effects on activity. The activity of a compound is based on the

structure. Single point mutations in peptide sequences can lead to divergent activities. Rudinger *et al.* (Peptide Hormones, **1976**, 1-7, see the conclusions in particular) state "The significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from the case to case by painstaking experimental study." It has been shown in numerous peptides that a single amino acid can have deleterious effects on the peptide. For example, Bradley *et al.* (*J. Mol. Biol.*, **2002**, *324*, 373-86) teach that a singe substation of Ala ->Gly in six analogous structural peptides of an ankyrin protein resulted in dramatic and diverse effects on protein stability.

Furthermore, it is unclear if the claimed compound will retain their activity *in vivo* against the different types of cancer. The state of the art regarding the treatment of cancer and the inhibition of angiogenesis is fraught with problems. One cannot conclude, based on even animal models, that a drug will be effective *in vivo* in human patients. Immunotherapy's killing power of the transformation of 3T3 cells by a mutated protooncogene, simply does not have the same significance for cells *in vivo*. Clonogenic assays are not always helpful since they "can't always predict how a tumor will respond to a drug in an animal" and "[s]ometimes they don't work because the cells simply fail to divide in culture." (See page 1042 of Gura). In essence, the art indicates "rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer or diseases of the central nervous system." (See page 44 of Golden). Further, tumor angiogenesis, wound angiogenesis, and eye angiogenesis involve different mechanism due to the different proteins involved in capillary formations in wounds and tumors. Thus, given the problems associated with the treatment of cancer and inhibition of angiogenesis, and one would be burdened to practice the claimed invention with undue experimentation.

Finally, the specification fails to present working examples of compounds effective at treating autoimmune or infectious diseases. The specification describes in general terms that compounds of the invention can be useful in treating both classes of disease. The nature of autoimmune diseases which include multiple sclerosis, Type II Diabetes and rheumatoid arthritis, in particular is exceptionally complex and unpredictable. The nature of infectious diseases, which include human immunodeficiency virus, is likewise complex and unpredictable. Thus, in the absence of specific guidance and working examples, the skilled artisan would be burdened to practice the claimed invention with undue experimentation.

*The quantity of experimentation necessary*

Since, the art indicates a level of unpredictability in treating cancer, autoimmune disorders and infectious diseases is high and the instant specification provides very little guidance on the treatment of cancer or any disease known to man, one would be burdened with undue experimentation to practice the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

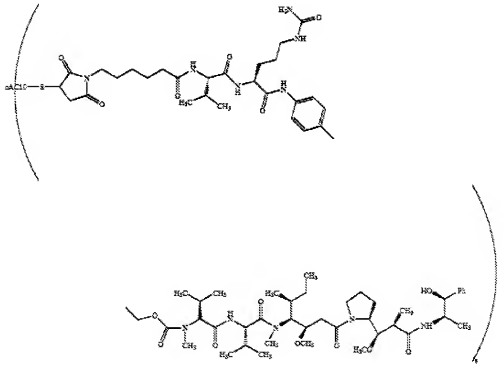
9. Claims 1, 2, 7, 17-19, 20, 21, 27, 111-121 and 123 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the connectivity between R4 and R5 and the backbone when $R^4$ and $R^5$ join and the connectivity between $(CR^aR^b)_n$ and the formula when $R^4$ and $R^5$ join.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, 121 and 123 are rejected under 35 U.S.C. 102(e) as being anticipated by Law *et al.* (U.S. Publication No,. 2005/0123536). Law *et al.* teach the compound:



which is identical to the compound of claim 79 wherein p is 8 and L is a monoclonal antibody against the CD30 antigen (example 5).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

***Double Patenting***

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-44 and 48-103 of copending Application No. 11/833,954. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 1-44 and 48-103 of copending Application No. 11/833,954 represent subgenera that

anticipate claims 1 and 7 of the instant application. The antibody-drug conjugate of claim 17 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claim 9. The antibody-drug conjugates of claim 4-44 of copending Application No. 11/833,954 represents subgenera that anticipates instant claim 17. The antibody-drug conjugates of claim 33 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claim 18. The antibody-drug conjugates of claim 72 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claims 20 and 120. The antibody-drug conjugates of claim 72 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claims 21 and 27. The antibody-drug conjugates of claim 102 of copending Application No. 11/833,954 overlap in scope with instant claims 54, 66 and 79. The antibody-drug conjugates of claim 72 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claim 121. The pharmaceutical composition of claim 45 of copending Application No. 11/833,954 represents a subgenus that anticipates instant claim 111. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 and 40-89 of copending Application No. 11/833,959. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 1-37 and 40-90 of copending Application No. 11/833,954 represent subgenera that anticipate and/or overlap in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 112, 113 and 116 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 11/833,961. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of claims 1-54 of copending Application No. 11/833,961 represent subgenera that anticipate and/or overlap in scope with claims 112, 113 and 116 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 112, 113 and 116 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 11/833,964. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of claims 1-54 of copending Application No. 11/833,964 represent subgenera that anticipate and/or overlap in scope with claims 112, 113 and 116 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 12/016,978. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claim 11 of copending Application No. 12/016,978 represents a subgenus that anticipates and/or overlaps in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 112, 113 and 116 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8 and 9 of copending Application No. 10/558,811. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of claims claims 8 and 9 of copending Application No. 10/558,811 represent subgenera that anticipate and/or overlap in scope with claims 112, 113 and 116 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 74-94, 109 and 222-235 of copending Application No. 10/983,340. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 74-94, 109 and 222-235 of copending Application No. 10/983,340 represent subgenera that anticipate and/or overlap in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 11/667,437. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 1-18 of copending Application No. 11/667,437 represent subgenera that anticipate and/or overlap in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application.

Claims 111-114, 116, 117 and 119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-30 of copending Application No. 11/667,437. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical compositions and methods of claims 19-30 of copending Application No. 11/667,437 represent subgenera that anticipate and/or overlap in scope with claims 111-114, 116, 117 and 119 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

21. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-99 of copending Application No. 11/994,459. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 53-99 of copending Application No. 11/994,459 represent subgenera that anticipate and/or overlap in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application.

Claims 111-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 100-134 of copending Application No. 11/994,459. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical compositions and methods of claims 100-134 of copending Application No. 11/994,459 represent subgenera that anticipate and/or overlap in scope with claims 111-119 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

22. Claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-73 of copending Application No. 11/994,809. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of claims 28-73 of copending Application No. 11/994,809 represent subgenera that anticipate and/or overlap in scope with claims 1, 2, 7, 9, 17-21, 27, 54, 66, 79, 111, 120, and 121 of the instant application.

Claims 111-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 74-109 of copending Application No. 11/994,809. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical compositions and methods of claims 74-109 of copending Application No. 11/994,809 represent subgenera that anticipate and/or overlap in scope with claims 111-119 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Claims 112, 113 and 116 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application No. 11/677,029. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of claims 1-40 of copending Application No. 11/677,029 represent subgenera that anticipate and/or overlap in scope with claims 112, 113

and 116 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday, Tuesday, Thursday, and Friday, 8:30 A.M. to 3:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Cmb

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